### II. ARGUMENTS AND REMARKS

## 1. Rejection under 35 USC § 112 should be withdrawn

Claim 81 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, allegedly because the metes and bounds of the term "the oligonucleotide or thereof" in line 1 of claim 81 cannot be determined.

Applicants amend claim 81 with this response to recite that the oligonucleotide is GTTAGGGTTAG. The term "or thereof" is deleted from the claim. Amended claim 81 particularly points out and distinctly claims the subject matter which applicant regards as the invention. Therefore, the rejection of claim 81 under 35 U.S.C. §112, second paragraph may be properly withdrawn and withdrawal is respectfully requested.

### 2. Claim Rejection under 35 USC § 102 should be withdrawn

Claim 83 stands rejected under 35 U. S. C. 102(b) allegedly as being anticipated by Norton et al (Nature Biotech., Vol. 14, pages 615-619,1996).

Applicants cancel claim 83 with this response and therefore, the rejection of claim 83 is moot.

### 3. Claim Rejections under 35 USC § 103 should be withdrawn

Claims 78-83 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hitoshi et al (US 2002/0027167) in view of Norton et al (Nature Biotech., Vol. 14, pages 615-619,1996)) and Page et al. (Exp'l. Cell Res., Vol. 252, pages 41-49,1999).

The Examiner characterized the claims as being directed to compositions

comprising an oligonucleotide comprising between 1-20 increments of TTAGGG, optionally comprising GTTAGGGTTAG, or comprising at least 50% identity with these motifs, wherein the first nucleotide linkages on the 3'-end are hydrolyzable by a 3'-5' nuclease, and which oligonucleotide further comprises non-hydrolyzable linkages, which are optionally phosphorothioate internucleotide linkages, or which oligonucleotide is optionally a PNA.

The Examiner alleges that *Hitoshi et al* (US 2002/0027167) teach nucleic acids encoding the nuclease MRE11 and recombinant MRE11. The Examiner agrees that *Hitoshi* does not teach the synthetic substrate sequences and the modifications instantly claimed. Thus, *Hitoshi* does not teach or suggest the subject matter of the pending claims.

Page et al. teach compositions comprising a choice of various oligonucleotides with at least one increment of an oligonucleotide with at least 50% sequence identity with TTAGGG, which oligonucleotides also comprise non-hydrolyzable phosphorothioate internucleotide linkages for stability from nuclease degradation.

Unlike the *Page* oligonucleotides, the oligonucleotides recited by the pending claims comprise two different linkages: non-hydrolyzable internucleotide linkages and also hydrolysable linkages. The *Page* goal was to develop oligonucleotides with linkages that would be protected from nuclease degradation. In contrast to *Page*, the oligonucleotides recited by the pending claims are oligonucleotides that are substrates to a 3 to 5 nuclease. See claims 78 and 79.

To summarize, *Hitoshi* discloses Mre11 nuclease and *Page* discloses oligonucleotides that cannot be hydrolyzed by any nuclease. Thus, the combination of references cannot properly render obvious the pending claims.

The Examiner has added *Norton* to the *Hitoshi/Page* combination. But the Examiner agrees that *Norton* discloses a PNA and Applicants delete claim 83 that recite a PNA with this response. In connection with pending claims 78-82, *Norton* does not remedy the deficiencies of *Hitoshi and Page* discussed above and the *Hitoshi/Norton/Page* combination does not make the pending claims obvious because the combination fails to teach or suggest at least some of the elements as recited by the pending claims and therefore, the *prima facie* case of obviousness has not been established.

# III. CONCLUSION

Applicants respectfully submit that the instant application is in good and proper order for examination on the merits and early notification to this effect is respectfully solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at (312) 846-5622.

Respectfully submitted,

**HOWREY LLP** 

Dated: December 15, 2009

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